

# ANNUAL REPORT 2018

## CENTER FOR CLINICAL EPIDEMIOLOGY

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Region of  
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UNIVERSITY OF SOUTHERN DENMARK

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# WELCOME

We welcome everybody with an interest in clinical epidemiology and data analysis. We ask anyone with a project, advisory task or research project, in the need of assistance within clinical epidemiology and data analysis, to contact us:

Bente Mertz Nørgård – [bente.noergaard@rsyd.dk](mailto:bente.noergaard@rsyd.dk), Susanne Møllerstrøm – [susanne.moellerstroem@rsyd.dk](mailto:susanne.moellerstroem@rsyd.dk).

The vision of Center for Clinical Epidemiology is to be known and respected for projects and research within clinical epidemiology at an international level, and to provide expert knowledge within a wide range of diseases and clinical epidemiological methods to solve issues regarding the prognosis for patients. We want the staff at the Center for Clinical Epidemiology to be desirable collaborators in local, regional, national, and international projects and research activities.

Our mission is to ensure correct diagnosis and treatment of patients through research results and thereby to ensure that all clinical decisions in the treatment processes are evidence based. We want to focus especially on research findings that can be applied and implemented in the daily clinical practice.

Center for Clinical Epidemiology handles the following activities:

1. Special projects and consultancy services within clinical epidemiology and data analysis
2. Clinical epidemiological research and academic work

Apart from the above activities, the center houses and supports tasks for the RKKP (the regional clinical quality program - the Danish Clinical Registries).

In 2018 we published 29 peer reviewed articles in international medical journals, and we have brought external fundraising into a special focus of interest.

Bente Mertz Nørgård

Professor and head of Center for Clinical Epidemiology and the Research Unit of Clinical Epidemiology

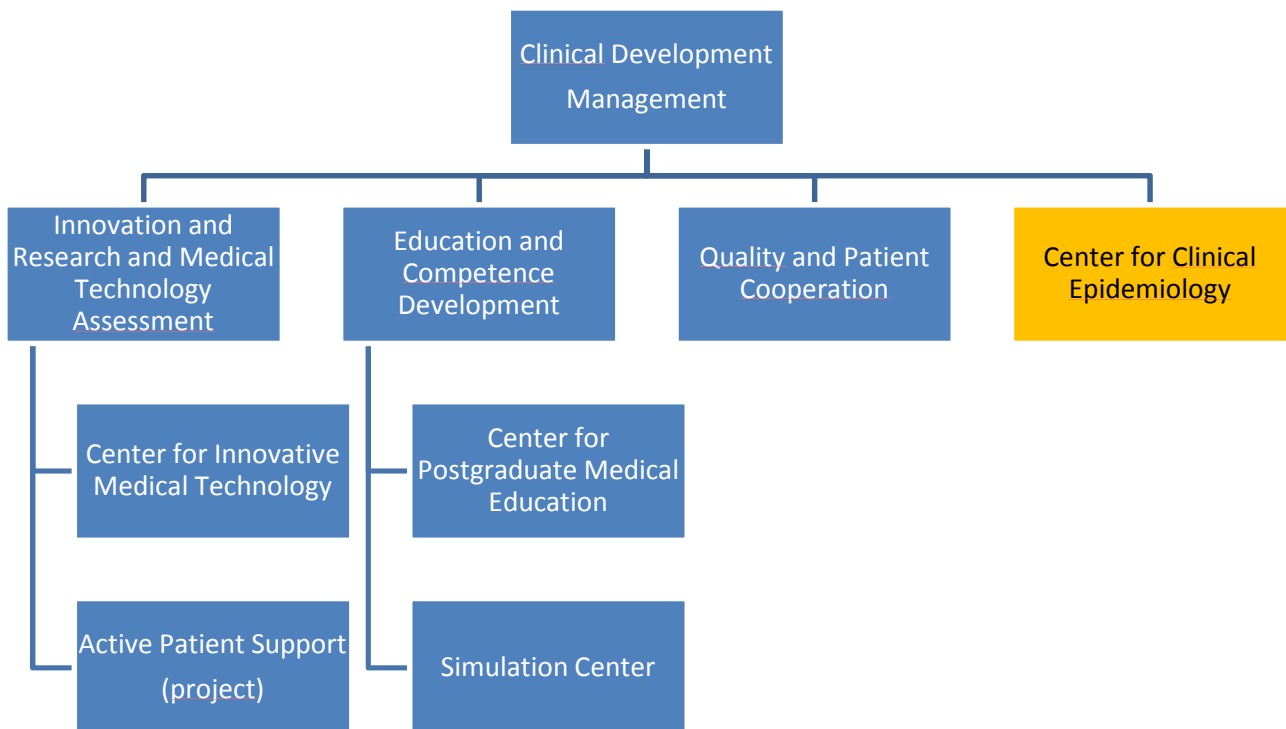
# ORGANIZATION

The center is affiliated with the Department of Clinical Development, Odense University Hospital, as an independent unit and all research activities from the research unit refer to the Department of Clinical Research, University of Southern Denmark.

An executive coordinating group is associated with the Center for Clinical Epidemiology with representatives from the management in the Region of Southern Denmark (chief of staff), the University of Southern Denmark (head of the Department of Clinical Research), and Odense University Hospital (chief of staff).

An overview of the staff at the Center for Clinical Epidemiology is available at our web-site: [www.ouh.dk/cke](http://www.ouh.dk/cke)

## Clinical Development



# WORKING RELATIONS

Activities within the following special projects and consultancy tasks in particular have occupied the center's resources in 2018 (the following is not a complete list of consultancy functions):

Center for Clinical Epidemiology has provided the Danish Clinical Registries (RKKP) with a number of consultancy services in 2018. The support has been given within the area of clinical epidemiology to a number of national clinical databases. CKE will also provide RKKP with consultancy services in 2019.

The cooperation with Emergency Medicine, Odense University Hospital, concerning the daily operation of "The emergency cohort of Southern Denmark" has been ongoing for several years. The database comprises data on all patients admitted via the Emergency Medicine Units in the Region of Southern Denmark, and the project is based on a cooperation with Professor Annmarie Lassen established in 2012.

Many staff members in the Center for Clinical Epidemiology handled consultancy tasks for a number of external parties locally, regionally and nationally, all within clinical epidemiology and data analysis. For instance: A consultancy agreement on a project on antibiotic use, with the Focused Research Unit in Emergency Medicine, Institute of Regional Health Research, University of Southern Denmark, was inaugurated in 2017. Data from all acutely admitted patients were collected, followed by six months of implementing an antibiotic stewardship program, and finalized by another six months of data collection from all acutely admitted patients. Data comprising variables of microbiology, antibiotics, and clinics were compiled and analyzed by our employees.

A consultancy agreement with the Department of Infectious Diseases, Odense University Hospital, was established in 2017. The agreement involves statistical, epidemiological, and data management support to different infectious disease projects, e.g. tuberculosis in HIV patients in Ghana, hepatitis C in drug users, and sepsis biomarkers, to name a few. The collaboration was continued in 2018.

We have an advisory cooperation with Rygcenter Middelfart (Research Department Spine Centre of Southern Denmark, Hospital Lillebaelt, Middelfart) on two main projects:

- Incidence and regional variation of Morbus Bechterew and Spondyloarthritis from 2000-2013: A nationwide cohort study. The aim of the study is to describe the incidence of ankylosing spondylitis and spondyloarthritis in the Danish population from 2000-2013, for the whole nation and for each of the five regions to evaluate if there is a trend over time explained by use of magnetic resonance imaging.
- Prognostic factors of the patients' course when referred to the Spine Centre of Southern Denmark for decision support. The aim of this project is to describe a course of disease and the effect of prognostic factors in the process. Based on the identified prognostic models algorithms are set up to develop individually adapted decision support tools.

**Regarding all working partners related to research projects please see the chapter "Research activities".**

# RESEARCH ACTIVITIES

**The Research Unit of Clinical Epidemiology** was established in 2009 with the purpose of handling all research and academic activities in the center. The unit is academically affiliated with the Department of Clinical Research at the University of Southern Denmark.

Several of the employees at the Center for Clinical Epidemiology have a formal academic employment at the Department of Clinical Research. We have a clinical professorship which is also linked to the daily management at the center, and academic affiliations (lecturer/adjunct) of two biostatisticians and two clinical epidemiologists.

The professor of the department is also nominated as Senior Epidemiologist at the Brigham and Women's Hospital, Boston, and lecturer, part-time, at Harvard Medical School.

The Research Unit of Clinical Epidemiology has affiliated an adjunct professor in clinical epidemiology (Sonia Friedman, MD, Visiting Professor Harvard Medical School and Brigham and Women's Hospital, Boston). Sonia Friedman is an expert within chronic inflammatory bowel disease and reproduction issues. At the same time Sonia Friedman is an associated professor at Harvard University, Boston.

The Research Unit of Clinical Epidemiology has also affiliated Pedro Manuel Sarmiento Rodrigues Póvoa, Unidade de Cuidados Intensivos Polivalente, MD, Hospital de São Francisco Xavier, Lisbon, as an adjunct professor. Pedro Póvoa is an expert researcher within areas related to intensive care and patients suffering from sepsis. Pedro Póvoa has especially focused on the importance of C-reactive protein of which daily records exceed a single count in monitoring the patient's condition.

The employees at Center for Clinical Epidemiology conduct their own initiated research projects in collaboration with domestic and foreign researchers. Our research is mainly

within the following areas (for the specific publications please refer to the last chapter 'Publications'):

Cancer

Acute medicine and intensive care

Sepsis

Bowel diseases and chronic inflammatory bowel disease

Human reproduction

Chronic diseases

Obstetrics

Gynecology

Psychiatrics

Geriatrics

Social medicine

### **Presentations and congresses**

- "OPEN's 10 year Anniversary Seminar" December 6th 2018 in "Klinikbygningen" OUH Odense University Hospital
- Open Research, Region of Southern Denmark, April 23, 2018. Oral presentation based on: Elective abortions in women with inflammatory bowel disease (by Bente Mertz Nørgård, Bjarne Magnussen, Jens Fedder, Punyanganie S. de Silva, Sonja Wehberg, Sonia Friedman).
- Open Research, Region of Southern Denmark, April 23, 2018. Oral presentation based on: Do biomarker levels and their changes in adult haematological malignancy patients mainly reflect infectious episodes and what is their prognostic utility? (by Gradel, K.O., Póvoa, P., Garvik, O.S., Ljungdalh, P.M., Gram-Hansen, P., Lassen, A.T., Jensen, T.G., Kolmos, H.J., Pedersen, C., Nielsen, S.L., Vinholt, P.J., Frederiksen. H. .



- Composite variables in medical research - Bispebjerg Hospital 20 September 2018.
- Nordic IBD congress, 10 -12 October, 2018, Malmø. Oral presentation: Selected reproductive issues in patients with IBD
- DCCC PRO gruppen, Sandbjerg gods, 19-20 November, 2018

# PHD-STUDENTS

## **Phd-students supervised by Center for Clinical Epidemiology staff members, 2018**

- Heidi Kammerlander: Biologic therapy during pregnancy in inflammatory bowel disease – clinical epidemiologic aspects focusing on use, treatment regimes, disease activity and safety during pregnancy. Public defence January 2018.
- Line Riis Jølving: Maternal chronic disease during pregnancy and long-term morbidity in the offspring. Public defence February 2018.
- Majken Munk Brønserud: Patientrapporteret livskvalitet hos lungecancer patienter – Anvendelse af patientrapporterede oplysninger (PRO) som kvalitetsindikator (Patient reported quality of life in patients with lung cancer – Applied patient reported information as a quality indicator). Ongoing.
- Ken Lund: Disease control in pediatric and adolescent patients with inflammatory bowel disease: aspects of Anti-TNF- $\alpha$  and physical activity. Ongoing.
- Pernille Sanberg Ljungdahl: Psychiatric comorbidity in Back Pain Disorders – Risk, treatment and pharmaco-epidemiological analysis. Ongoing.

# ACADEMIC ASSESSMENT

In 2018 the staff at the Center for Clinical Epidemiology has

- worked as reviewers for scientific journals
- evaluated research protocols for local, national, and international scientific foundations
- participated in scientific congresses nationally and internationally
- given scientific oral presentations nationally and internationally
- undertaken assessments of PhD protocols and dissertations for the Faculty of Health Sciences at the University of Southern Denmark and other universities in Denmark
- acted as chairman of the evaluation committee of PhD dissertations
- acted as board member of the evaluation committee for a clinical professorship
- been appointed as censor
- undertaken censorship tasks for the medical educations in Denmark
- supervised PhD students

# TEACHING

The staff at the center has trained, supervised, and examined a large number of bachelor students and master's thesis students at the Faculty of Health Sciences at University of Southern Denmark.

The staff has participated in Multiple Mini Interview (MMI) interviews, kvote 2, medicine. The staff has taught 'Introduction to epidemiology and register based research in Denmark' at the pre-PhD course at University of Southern Denmark.

# FUNDINGS

Beckett-fonden: Topic: Assisted reproduction in thyroid diseases.

The Region of Southern Denmark, free funds. Topic: Assisted reproduction treatment and disease activity.

The Region of Southern Denmark, free funds. Topic: Diagnosis, treatment and survival of biliary tract cancer in Denmark

Scleroseforeningen (Danish MS Society). Topic: Assisted reproduction and multiple sclerosis.

Kong Christian den Tiendes Fond (King Christian 10<sup>th</sup> Foundation). Topic: Assisted reproduction and chronic disease.

OUH (Odense University Hospital), free funds. Topic: Biologic therapy and short term outcomes.

OUH (Odense University Hospital), free funds. Assisted reproduction and multiple sclerosis.

Brigham and Women's Hospital, Boston. Topic: Studies on inflammatory bowel disease, reproduction and biologic therapy.

# PUBLICATIONS

## Scientific publications

In 2018, 29 papers were published in peer-reviewed journals. Please refer to **the list below** or our web-site [http://findresearcher.sdu.dk/portal/en/organisations/klinisk-epidemiologi\(ad64bacf-78d9-4b18-84a3-53070d6bc23a\)/publications.html?filter=researchhttp%3A%2F%2F](http://findresearcher.sdu.dk/portal/en/organisations/klinisk-epidemiologi(ad64bacf-78d9-4b18-84a3-53070d6bc23a)/publications.html?filter=researchhttp%3A%2F%2F)

1. Ryg J, Engberg H, Mariadas P, Pedersen SGH, Jorgensen MG, Vinding KL, Andersen-Ranberg K. Barthel Index at hospital admission is associated with mortality in geriatric patients: a Danish nationwide population-based cohort study. *Clinical Epidemiology* 2018;10:1789-1800
2. Jølving LR, Nielsen J, Kesmodel US, Nielsen RG, Beck-Nielsen SS, Nørgård BM. Children Born by Women with Rheumatoid Arthritis and Increased Susceptibility for Chronic Diseases: A Nationwide Cohort Study. *Arthritis Care Res (Hoboken)*. 2018 Aug;70(8):1192-1197
3. Jølving LR, Nielsen J, Kesmodel US, Nielsen RG, Nørgård BM, Beck-Nielsen SS. Chronic diseases in the children of women with maternal thyroid dysfunction: a nationwide cohort study. *Clin Epidemiol*. 2018 Sep 28;10:1381-1390
4. Kammerlander H, Nielsen J, Kjeldsen J, Knudsen T, Gradel KO, Friedman S, Nørgård BM. Fecal calprotectin during pregnancy in women with moderate-severe inflammatory bowel disease. *Inflamm Bowel Dis* 2018; 24:839-848
5. Larsen MD, Friedman S, Magnussen B, Nørgård BM. Birth Outcome of Children Fathered by Men Treated with Systemic Corticosteroids during the Conception Period - A Cohort Study based on Nationwide Data. *Basic Clin Pharmacol Toxicol*. 2018 Jan;122(1):133-138
6. Friedman S, Larsen MD, Magnussen B, Jølving LR, de Silva P, Nørgård BM. Paternal use of azathioprine/6-mercaptopurine or methotrexate within 3 months before conception and long-term health outcomes in the offspring – a nationwide cohort study. *Letter. Reprod Toxicol*. 2018 Jan;75:147
7. Hansen S, Rasmussen BK, Laursen RJ, Kosteljanetz M, Schultz H, Nørgård BM, Guldborg R, Gradel KO. Treatment and survival of glioblastoma patients in Denmark: The Danish Neuro-Oncology Registry 2009-2014" has been accepted for publication in *Journal of Neuro-Oncology*. DOI 10.1007/s11060-018-2892-7
8. Friedman S, Magnussen B, Aoibhlinn O'Toole, Fedder J, Larsen MD, Nørgård BM. Increased use of medications for erectile dysfunction in men with ulcerative colitis and Crohn's disease compared to men without inflammatory bowel disease – a nationwide cohort study. *Am J Gastroenterol*. 2018 Jul 10. doi: 10.1038/s41395-018-0177-6.
9. Jølving LR, Nielsen J, Kesmodel US, Nielsen RG, Nørgård BM, Beck-Nielsen SS. Maternal thyroid dysfunction and chronic diseases in their children - a nationwide cohort study. *Clinical Epidemiology* 2018:10 1381–1390

10. Nørgård BM, Magnussen B, Fedder J, de Silva P, Wehberg S, Friedman S. The risk of elective abortion in women with Crohn's disease and ulcerative colitis: A nationwide cohort study. *Inflamm Bowel Dis*. 2018 Aug 10. doi: 10.1093/ibd/izy263
11. Nørgård BM, Larsen MD, Friedman S, Knudsen T, Fedder J. Decreased chance of a live born child in women with rheumatoid arthritis after assisted reproduction treatment– a nationwide cohort study. Accepted in the *Annals of the Rheumatic Diseases* December 2018
12. Nørgård BM, Jølvig LR, Larsen MD, Friedman S. Parental IBD and long-term health outcomes in the offspring. Accepted in *Inflamm Bowel Dis* December 2018
13. Bay-Richter C, Buttenschøn HN, Mors O, Eskelund A, Budac D, Kærlev L, Wegener G. Latent toxoplasmosis and psychiatric symptoms - A role of tryptophan metabolism? *J Psychiatr Res*. 2018 Dec 17;110:45-50
14. Iachina M, Ljungdalh PM, Sørensen RG, Kaerlev L, Blaakær J, Trosko O, Qvist N, Nørgård BM. Influence of Prior Psychiatric Disorders on the Treatment Course of Gynaecological Cancer - A Nationwide Cohort Study. *Clin Oncol (R Coll Radiol)*. 2018 Nov 27. pii: S0936-6555(18)30502-8. doi: 10.1016/j.clon.2018.11.006. [Epub ahead of print]
15. Kaerlev L, Iachina M, Trosko O, Qvist N, Ljungdalh PM, Nørgård BM. BMC Cancer. Colon cancer patients with a serious psychiatric disorder present with a more advanced cancer stage and receive less adjuvant chemotherapy - A Nationwide Danish Cohort Study. 2018 Oct 29;18(1):1050
16. Ugelvig Petersen K, Volk J, Kaerlev L, Lyngbeck Hansen H, Hansen J. Cancer incidence among merchant seafarers: an extended follow-up of a Danish cohort. *Occup Environ Med*. 2018 Aug;75(8):582-585
17. Laouali N, Pilorget C, Cyr D, Neri M, Kaerlev L, Sabroe S, Gorini G, Richiardi L, Morales-Suárez-Varela M, Llopis-Gonzalez A, Ahrens W, Jöckel KH, Afonso N, Eriksson M, Merletti E, Olsen J, Lyng E, Guénel P. Occupational exposure to organic solvents and risk of male breast cancer: a European multicenter case-control study. *Scand J Work Environ Health*. 2018 May 1;44(3):310-322
18. Hansen ÅM, Grynderup MB, Bonde JP, Conway PM, Garde AH, Kaerlev L, Kolstad HA, Mikkelsen S, Rugulies R, Thomsen JF, Willert M, Høgh A. Does Workplace Bullying Affect Long-Term Sickness Absence Among Coworkers? *J Occup Environ Med*. 2018 Feb;60(2):132-137
19. Wehberg, S., Guldberg, R., Gradel, K.O., Kesmodel, U.S., Munk, L., Andersson, C.B., Jølvig, L.R., Nielsen, J., Nørgaard, B.M. (2018): Risk factors and between-hospital variation of caesarean section in Denmark: a cohort study. *BMJ Open*, 8:e019120
20. Illum, N.O., Bonderup, M., Gradel, K.O. (2018): Parents' expressions of concerns and hopes for the future and concomitant assessments of disability in their children. *Clinical Medicine Insights: Pediatrics*, 2018 Jun 27; doi: 10.1177/1179556518784948. eCollection 2018
21. Larsen MD, Guldberg R, Lose G. Perioperative cardiovascular complications following urogynecological operations. *Acta obstetricia et gynecologica Scandinavica*. 2019;98(1):61-7
22. Strehlau AG, Larsen MD, Sondergaard J, Almarsdottir AB, Rosholm JU. General practitioners' continuation and acceptance of medication changes at sectorial transitions of geriatric patients - a qualitative interview study. *BMC family practice*. 2018;19(1):168

23. Friedman S, Magnussen B, O'Toole A, Fedder J, Larsen MD, Norgard BM. Increased Use of Medications for Erectile Dysfunction in Men With Ulcerative Colitis and Crohn's Disease Compared to Men Without Inflammatory Bowel Disease: A Nationwide Cohort Study. *The American journal of gastroenterology*. 2018
24. Weltz V, Guldberg R, Larsen MD, Magnussen B, Lose G. Influence of body mass index on short-term subjective improvement and risk of reoperation after mid-urethral sling surgery. *International urogynecology journal*. 2018;29(4):585-591.
25. Juul MB, Jensen PH, Engberg H, Wehberg S, Dessau-Arp A, Haziri D, Kristensen HB, Baech J, Schurmann L, Clausen MR, Valentin R, Knudsen LM, Munksgaard L, El-Galaly TC, Frederiksen H, Larsen TS. Treatment strategies and outcomes in diffuse large B-cell lymphoma among 1011 patients aged 75 years or older: A Danish population-based cohort study. *Eur J Cancer*. 2018 Aug;99:86-96
26. Jørgensen SL, Mogensen O, Wu C, Lund K, Iachina M, Korsholm M, Jensen PT. Nationwide introduction of robotic minimally invasive surgery in early-stage endometrial cancer and its influence on severe complications. *JAMA Surgery*, 2018
27. Gradel, K.O., Vinholt, P.J., Magnussen, B., Pedersen, C., Jensen, T.G., Kolmos, H.J., Lassen, A.T. (2018): Hypoalbuminemia as a marker of trans-capillary leakage in community-acquired bacteraemia patients. *Epidemiology and Infection*, 146, 648-655.
28. Gradel, K.O., Pova, P., Vinholt, P.J., Magnussen, B., Pedersen, C., Jensen, T.G., Kolmos, H.J., Lassen, A.T. (2018): Real-life data patterns of C-reactive protein and albumin level trajectories around bacteraemia. *Biomarkers in Medicine*, 12, 1251-1259.
29. Hansen, M.F., Lose, G., Sigurdardóttir, H.B., Gradel, K.O. (2018): A Danish national population-based cohort study of synthetic midurethral slings, 2007-2011. *International Urogynecology Journal*, in press.